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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/816,825	03/22/2001	Annette Bistrup	6510-107CON	7399

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Paula A. Borden
BOZICEVIC, FIELD & FRANCIS LLP
Suite 200
200 Middlefield Road
Menlo Park, CA 94025

EXAMINER	
RAO, MANJUNATH N	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 07/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/816,825	BISTRUP ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-36,38-43,45,55,57-61,63,65-75 and 77-96* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-36,38-43,45,55,57-61,63,65-75 and 77-96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4-14-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4-15-04 has been entered.

Claims 30-36, 38-43, 45, 55, 57-61, 63, 65-75, 77-96 are pending and now under consideration in this application.

Applicants' amendments and arguments filed on 4-15-04, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Specifically, the previous rejections under 35 U.S.C. 112, 2nd paragraph have been withdrawn in view of claim amendments. Examiner has also withdrawn the rejection of claims under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5-10 and 12 of U.S. Patent Application No. 10/007262, published as US 2002/0164748 A1 as applicants have shown that the conflicting claims have been cancelled in the co-pending application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30, 45, 55, 57, 58, 60, 61, 63, 65-69, 71-75, 77, 78-96, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for DNA with SEQ ID NO:1 encoding a full length polypeptide with SEQ ID NO:2 having glycosylsulfotransferase activity, or a polynucleotide that hybridizes to SEQ ID NO:1 under stringent conditions but encodes a polypeptide having glycosylsulfotransferase activity does not reasonably provide enablement for

1. any such DNA that is either 75%, 90%, or 95% identical to SEQ ID NO:1 and encoding a polypeptide with sulfotransferase activity or

2. any polynucleotides that comprises encodes a fragment of at least 25, 50, 100 a nucleotide sequence having 90% sequence identity to SEQ ID NO:1 encoding a glycosylsulfotransferase or

3. any polynucleotide sequence that encodes any fragment of at least 15, 50 amino acids of a polypeptide having at least 60% amino acid sequence identity to SEQ ID NO:2 or

4. any polynucleotide which encodes a fragment of 15, 50, 100, contiguous amino acids of SEQ ID NO:2 wherein said fragment exhibits sulfotransferase activity vectors and host cells comprising said polynucleotides and methods of making the encoded polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 30, 45, 55, 57, 58, 60, 61, 63, 65-69, 71-75, 77, 78-96 are so broad as to encompass any DNA which are fragments of SEQ ID NO:1 including variants mutants and recombinant fragments, and vectors and host cells comprising such DNAs and method of making the fragments of peptides encoded by said DNA. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNA sequences that are broadly encompassed by the claims.

The applicants propose to use the above polynucleotides for a variety of processes such as recombinant protein preparation, as hybridization probes, and research applications, diagnostic applications, therapeutic agent screening/discovery/preparation applications as well as therapeutic compositions (see pages 12-30). The nucleotide sequence determines the type of protein and the ultimate function of the encoded protein and only nucleic acids which encode a polypeptide with a specific activity can be envisioned as having any use.
Furthermore, since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence to obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. In other words, applicant needs to provide guidance as to which specific amino acids of the encoded polypeptide can be modified by way of deletion, substitution, addition etc. and in case of amino acid substitutions, which specific amino acids can be used to substitute the existing specific amino acids on the polypeptide sequence. However, in this case the disclosure is limited to the nucleotide sequence with SEQ ID NO:1

and encoded amino acid sequence of only a single glycosyl sulfotransferase-3, SEQ ID NO:2. The specification does not even teach a specific 25, 50 or 100 consecutive amino acids of SEQ ID NO:2 which exhibits the glycosylsulfotransferase activity let alone fragments of amino acids encoded by polynucleotides that are 75%, 90% or 95% identical to SEQ ID NO:1. Therefore, it would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides that are either 75%, 90%, or 95% identical to SEQ ID NO:1 and encoding a polypeptide with sulfotransferase activity; or any polynucleotides that encodes a fragment of at least 25, 50, 100 amino nucleotide sequence having percent sequence identity to SEQ ID NO:1 encoding a glycosylsulfotransferase; or any polynucleotide sequence that encodes any fragment of at least 15, 50 amino acids of a polypeptide having at least 60% amino acid sequence identity to SEQ ID NO:2 or 4. any polynucleotide which encodes a fragment of 15, 50, 100, contiguous amino acids of SEQ ID NO:2 wherein said fragment exhibits sulfotransferase activity vectors and host cells comprising said polynucleotides and methods of making the encoded polypeptides. The specification is limited to teaching the use of SEQ ID NO: 1 as encoding a polypeptide with SEQ ID NO:2 as a glycosylsulfotransferase but provides no guidance with regard to making variant polynucleotides vectors and host cells comprising such polynucleotides and also methods to use such polynucleotides or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polynucleotides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the

specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of SEQ ID NO:1, vectors and host cells comprising such polynucleotides because the specification does not establish: (A) regions of the polynucleotide encoding the protein glycosylsulfotransferase-3, which may be modified without affecting its function; (B) the general tolerance of polynucleotides encoding glycosylsulfotransferase-3 to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying specific nucleotide residues or in other words specific amino acid residues of the encoded polypeptide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including different variants of SEQ ID NO:1. The scope of the claims must bear

a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the claimed DNAs and determination of their use is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants have traversed the above rejection exhaustively arguing, in summary, that the specification enables the claimed invention. Applicants reiterate their argument that the specification teaches as to how to make the claimed nucleic acid and how to use the claimed nucleic acids. Applicants submit that the specification discusses various uses including use as probes primers to identify GST-3 and in diagnostic applications and to prepare GST-3 polypeptides using standard techniques. While reiterating what is claimed by them, applicants argue that court allows for considerable experimentation and that even then the only experimentation needed is to determine whether a given polypeptide fragment catalyzes transfer of a sulfate group from a sulfate donor to sulfate acceptor, all of which are explained in the specification and involve routine techniques. Examiner respectfully disagrees with such an argument as being persuasive to overcome the above rejection. While applicants may have taught assays for determining the sulfate transfer activity, what they have not taught is how to make the above claimed polynucleotides. For example polynucleotides which are 75%-95% identical to SEQ ID NO:1, i.e., where exactly those skilled in the art should make changes in the nucleotide sequence such that they are 75% identical to SEQ ID NO:1 but yet maintain all functional aspects. Applicants have also not taught as to how those skilled in the art would make polynucleotide encoding a polypeptide that is 60% identical to SEQ ID NO:2,

again --which specific amino acid residues can be changed without affecting the activity of the polypeptide—such that a polynucleotide encoding said polypeptide can be made using SEQ ID NO:1.. While the specification provides generalized guidelines, it very much lacks specific guidance regarding making changes to SEQ ID NO:1 or 2. Applicants argue that they have provided working examples of the use of polynucleotide fragments. Again all these are highly generalized and lack specifics especially with respect to SEQ ID NO:1 and 2.

While methods to produce variants of a known sequence, such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan, producing variants as claimed by applicants of a polynucleotide that is 2032 nucleotides in length requires that one of ordinary skill in the art be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. Hence the above rejection is maintained.

Claims 30, 45, 55, 60, 61, 63, 65-69, 71-75, 95, 96, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a

genus of DNA molecules which are fragments of SEQ ID NO:1 encoding fragments of SEQ ID NO:2.

These claims are directed to a genus of polynucleotides comprising fragments of SEQ ID NO:1 or polynucleotides encoding fragments of the amino acid sequence SEQ ID NO:2. As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The specification teaches the isolation and characterization of only a single species of the polynucleotide with SEQ ID NO:1 encoding the polypeptide with SEQ ID NO:2. Moreover, the specification fails to describe any other representative species by sufficient identifying characteristics or properties to show that applicant was in possession of the claimed genus. The identifying characteristics recited in above claims i.e., enzymatic activity, and the non-specific fragments of oligonucleotide/peptide sequences together include a description of function and a partial structural description of the claimed species, but does not include sufficient characteristics to limit the claimed genus to proteins which are not highly variable in both structure and function. The claims include species in which up to 70-80% of the

amino acid sequence or the nucleotide sequence of the single disclosed species has been substituted or modified. Therefore, the species within the genus are highly variable in structure. Thus for all the reasons discussed, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

In response to the previous Office action, applicants have traversed the rejection. Applicants have also amended the claims by including the functional property of the polypeptide and the polynucleotide. Therefore Examiner has withdrawn the previous rejection made for lack of written description. However, present claims, while providing specific functional aspects of the claimed polynucleotide continues to be directed to polynucleotides with meager or partial structural characteristics. Therefore, Examiner has made the above rejection. Examiner suggests cancellation of the above claims in order to move the application towards an allowance.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 30-36, 38-43, 45, 55, 57-61, 63, 65-75, 77-96 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,265,192. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim, because the examined claim is either anticipated by, or would have been obvious over the reference claim. See, e.g., *In re Berg*, 140 F.3d 1428,46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi* 759 F.2d 887,225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 30-36, 38-43, 45, 55, 57-61, 63, 65-75, 77-96 of the instant application and claims 1-6 of the reference patent are both directed to polynucleotides with SEQ ID NO:1 including variants mutants, recombinants and fragments of the same. A good number of different fragments of DNA claimed in the instant application and in the DNA in the reference patent are identical to one another. The portion of the specification (and the claims) in the reference patent that supports the recited polynucleotide includes several embodiments that would anticipate the fragments (i.e., fragments encoding peptides with or without any activity) claimed in claims 30-36, 38-43, 45, 55, 57-61, 63, 65-75, 77-96 herein. Claims of the instant application listed above cannot be considered patentably distinct over claims 1-6 of the reference patent when there is specifically recited embodiment that would anticipate mainly claims 30-36, 38-43, 45, 55of the instant application. Alternatively, claims 30-36, 38-43, 45, 55, 57-61, 63, 65-75, 77-96 cannot be considered patentably distinct over claims 1-6 of the reference patent when there is specifically disclosed embodiment in the reference patent that supports claims 1-6 of that patent and falls within the scope of claims 30-

36, 38-43, 45, 55, 57-61, 63, 65-75, 77-96 herein because it would have been obvious to one having ordinary skill in the art to modify claims 1-6 of the reference by selecting a specifically disclosed embodiment that supports those claims. One of ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being a preferred embodiment within claims 1-6 of the reference patent.

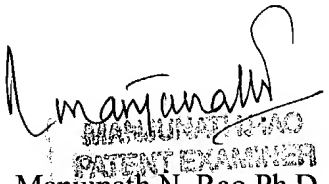
In their response to the previous Office action, applicants request withdrawal of the above rejection as they have enclosed a Terminal Disclaimer disclaiming patent term beyond the expiration date of US patent No. 6,265,192. However, no such T.D. was found enclosed. Therefore in view of the absence of a T.D. Examiner continues to maintain the above rejection for reasons of record.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.



Manjunath N. Rao Ph.D.
July 14, 2004